Japanese Encephalitis Virus Vaccine IC51

ERICH TAUBER

Japanese Encephalitis Virus vaccine IC51

OVERVIEW

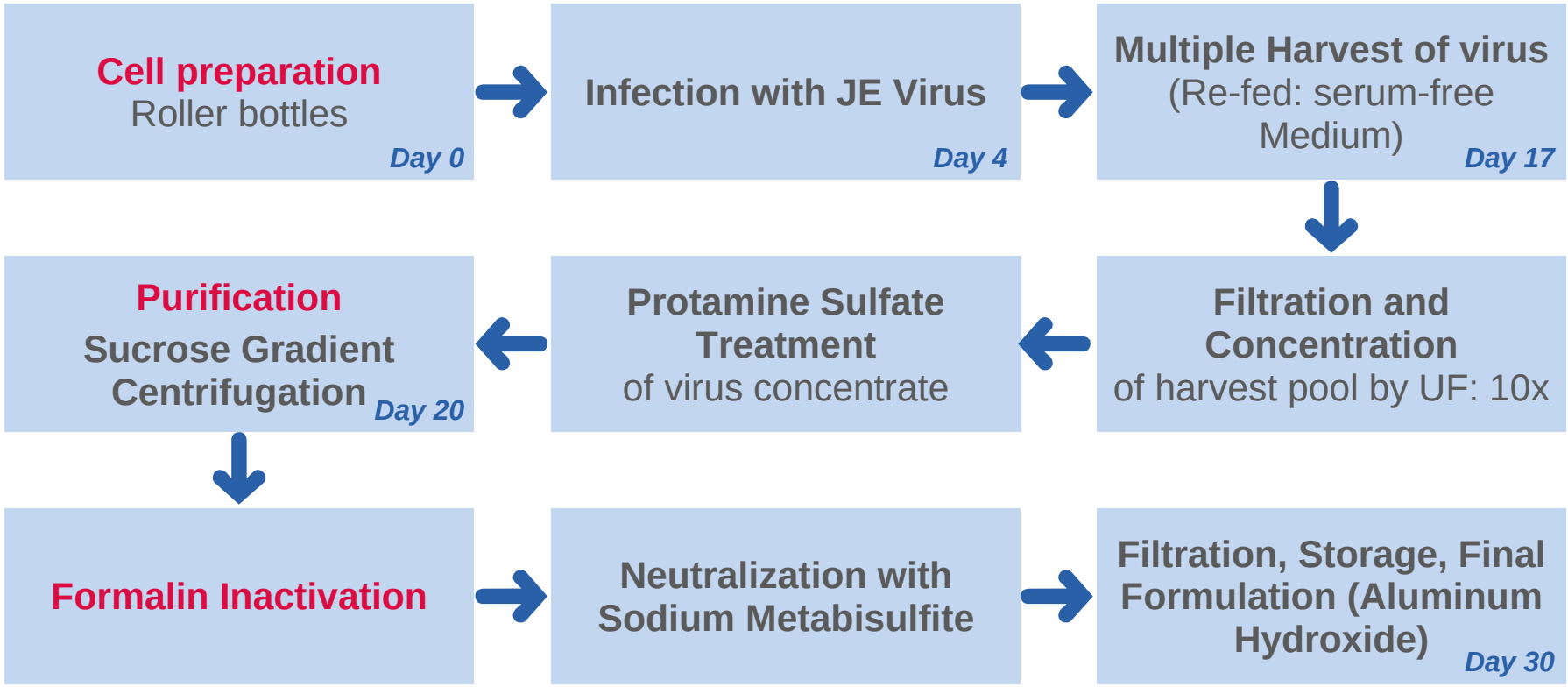
- IC51 is a second generation vaccine based on JEV strain SA_{14}-14-2
- This strain is used as a live virus vaccine in China
- Our vaccine is
  - produced in Vero cells
  - purified
  - inactivated
  - alum formulated

Development Progress as a Travelers Vaccine

OVERVIEW

- Phase 1 & 2 done in USA by Walter Reed Army Institute of Research
- Phase 3 started in 2005 US, EU and AUS
- Estimated Licensure:
  - US 2007
  - EU 2007 / 2008

IC51: Manufacturing Process Flow



JE Vaccines used in the Western World

Mouse Brain Derived, inactivated: Nakayama or Bejing strain

- JE-VAX®: Biken / Sanofi Pasteur
  - Licensed in US, Australia, Canada
- Korean Green Cross / Berna
- Denka Seiken
- Vaccination schedule:
  - s.c., day 0, 7, 30
  - accelerated: 0,7,14
  - Denka Seiken: 0,14 (180)
- costs: € 150 - 200,-

Licensure strategy for IC51 as a Travelers Vaccine

Efficacious vaccine is licensed in the Western world

- JE-VAX® showed vaccine efficacy of 91% (CI 70-97%)
  (Hoke *et al* 1988)

A classical field study is not feasible

- Placebo arm would be unethical (existing vaccine)
- Low incidence (because of existing vaccine) would make it prohibitively large:
  approx. 250,000 subjects to reproduce JE-VAX® licensure data
  (Markoff, 2000)

Licensure could be obtained on the basis of non-inferiority IC51 vs. JE-VAX® treatment arms:

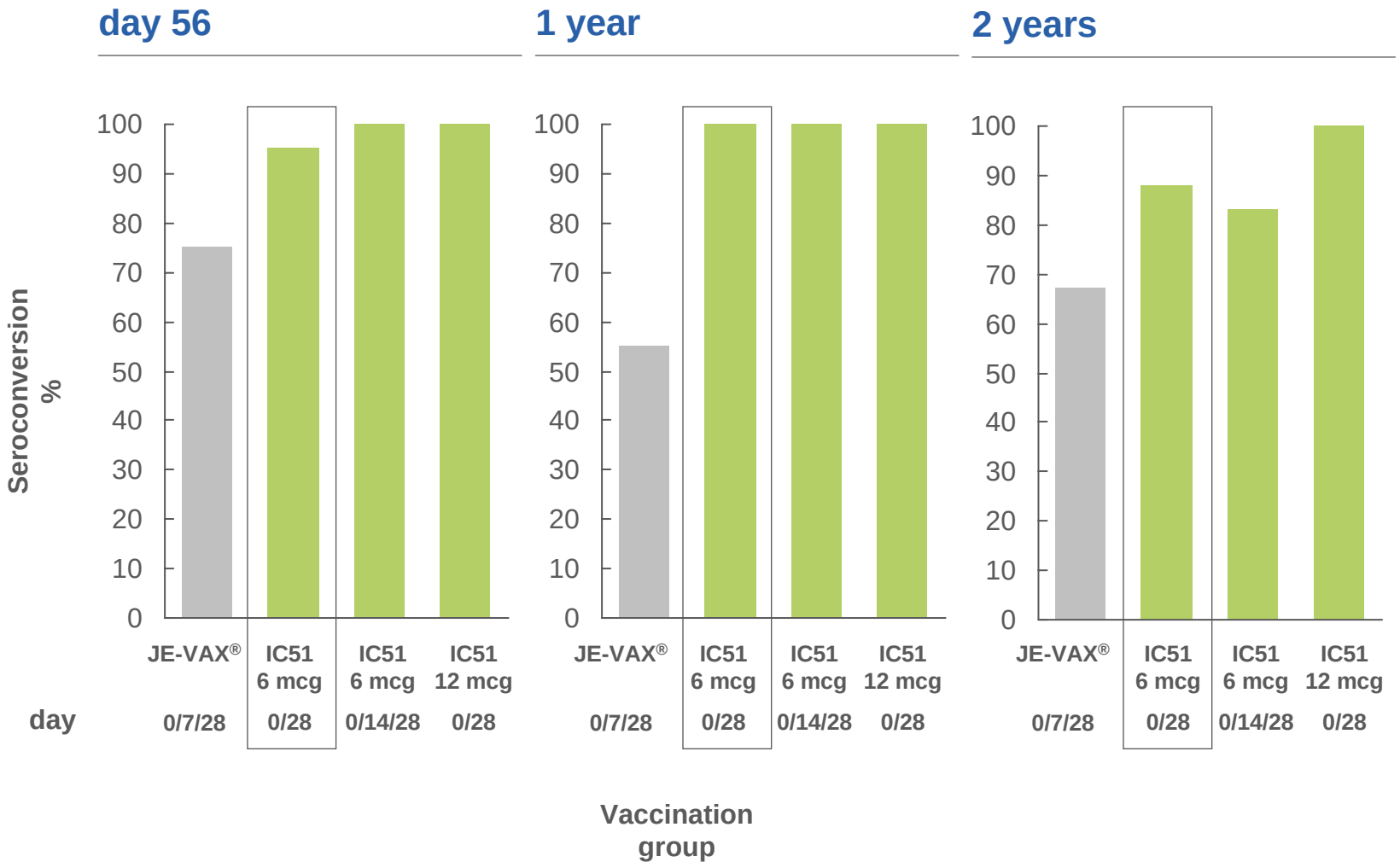
- Seroconversion rate (SCR)
- Geometric mean titers (GMTs)

Hoke *et al* 1988, New Eng. J. Med. 319:608-14

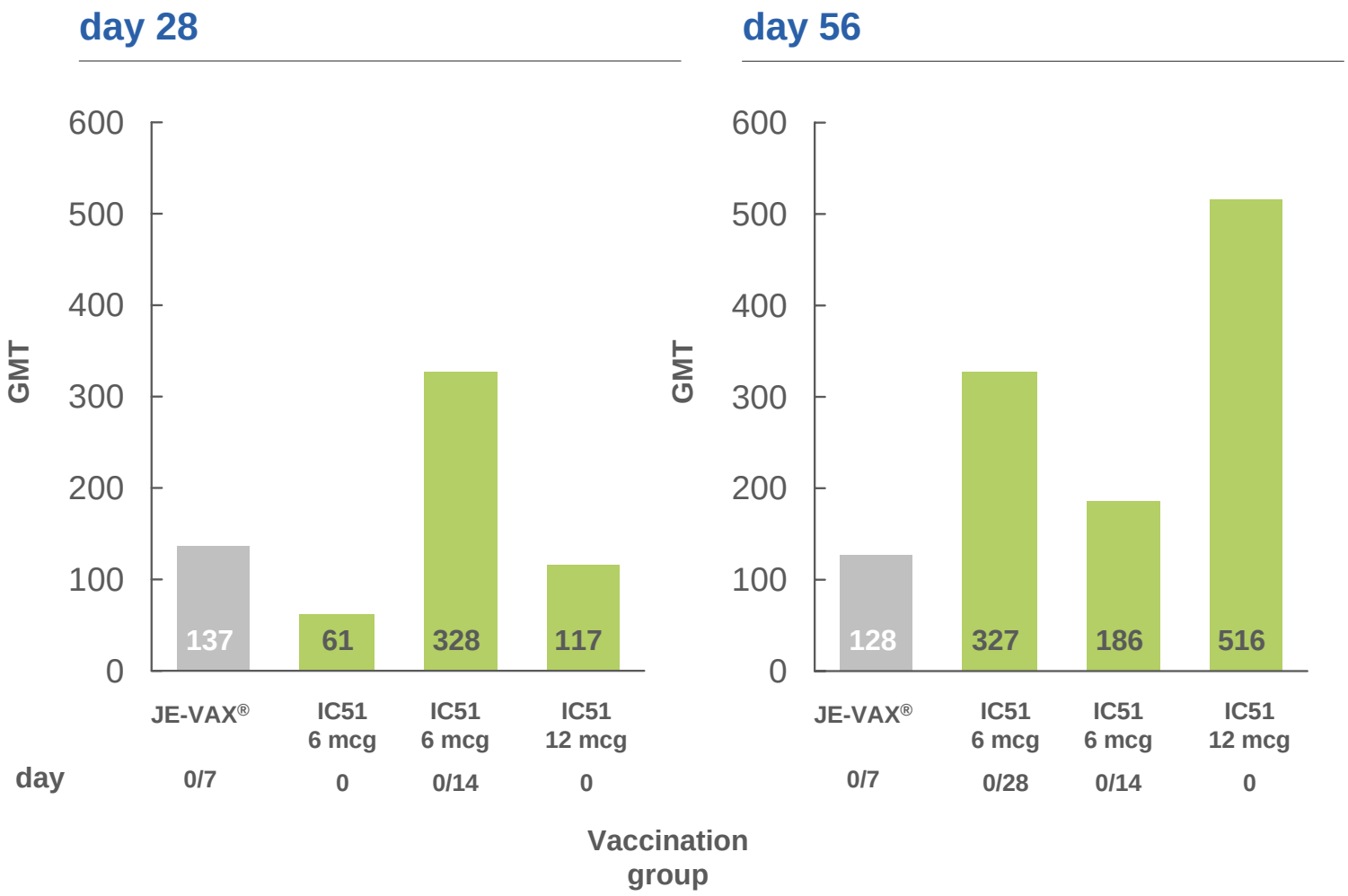
Markoff 2000, Vaccine 18:26-32

Phase 2: Immunogenicity Results

KINETICS OF SCR



Phase 2: Geometric Mean Titers (GMT)



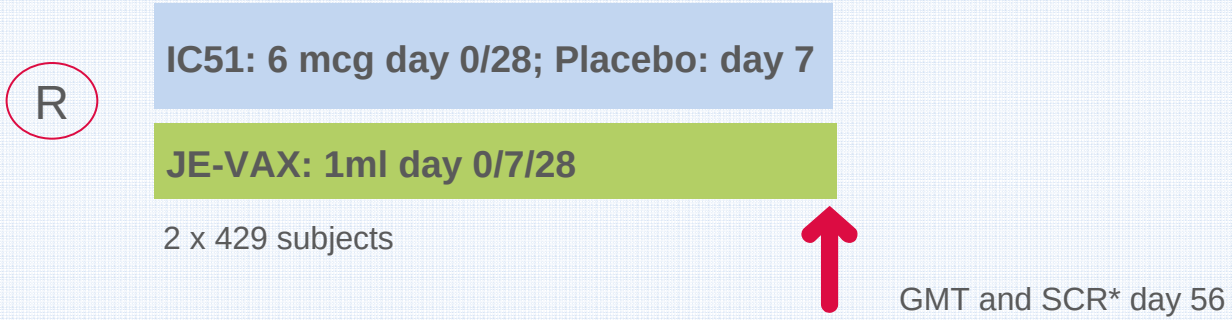
IC51 Phase 3 trial program

PHASE 3 PROGRAM TO ENROLL 4.900 SUBJECTS IN TOTAL

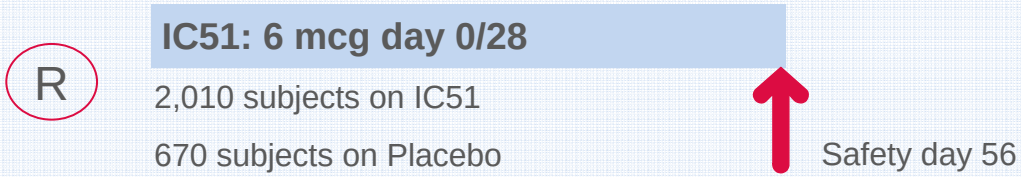
1. Pivotal Immunogenicity (IC51-301)
2. Pivotal Safety (IC51-302)
3. Long-term Immunogenicity (IC51-303)
4. Travelers (IC51-308)
5. Rapid Immunization (IC51-304)
6. Booster Study (IC51-305)
7. Batch Comparison (IC51-309)

IC51 Pivotal Immunogenicity and Safety Trials

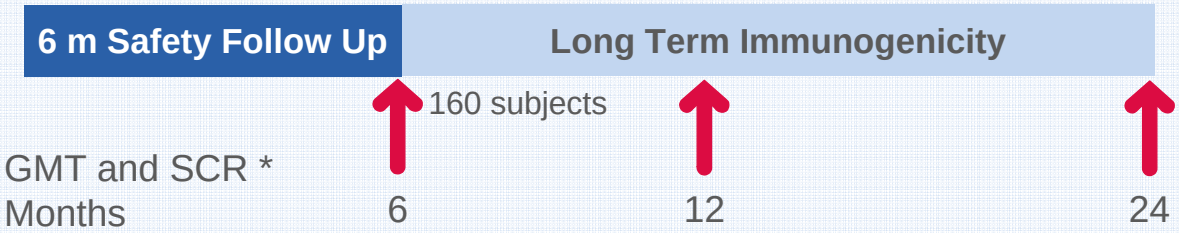
IC51-301 Non-Inferiority



IC51-302 Safety



IC51-303 Long Term Immunogenicity



R= Randomization

GMT= Geometric Mean Titers

SCR* = Seroconversion rate

Clinical trial IC51-301 met endpoint

FIRST RESULTS OF PIVOTAL PHASE 3 CLINICAL TRIAL

JEV was non-inferior to JE-VAX®

- » **SCR** ✓ (Seroconversion Rate)
- » **GMT** ✓ (Geometric Mean Titer)

Additional

- » **No safety concerns observed*** ✓

Full results will be presented at ASTMH. Data will be the foundation for license applications to FDA and EMEA**

*Interim analysis

**American Society of Tropical Medicine and Hygiene; Annual Meeting, Nov. 12-16,2006 in Atlanta

Development Timelines for Travelers Vaccine

» Phase 3 start	Q3 2006 ✓
» Pivotal Trials Completed	Q2, Q3 2006
» Regulatory Filing initiated	Q4 2006 / Q1 2007
» Market Launch US	2007
» Market Launch EU	2008

Intercell JEV Vaccine for endemic countries

MAKING THE VACINE AVAILABLE TO THOSE WHO NEED IT MOST

- Local partner for manufacturing and development: Biological E, Hyderabad, India
- Produce the vaccine locally, but with identical process and equipment as used for EU/US licensure
- Tailor final product to specific needs of the region

Development steps of novel JEV vaccine for endemic regions

Manufacturing → Clinical development → Regulatory approval → Distribution

Current status of JEV Vaccine development

- Partner in India for manufacturing the material for clinical development and commercialization
- Tech Transfer
- Manufacturing initiated

- Phase 1 to 3 trials performed in adults were successfully completed in non-endemic countries
- Phase 2 and 3 trials in children and adults in India under preparation

- Biological E is in the process of WHO pre-qualification for other vaccines
- seek national approval for relevant countries

- Intend to the make this vaccine for both private as well as public markets

An ideal JEV Vaccine for endemic regions

PROTECTING CHILDREN AS WELL AS ADULTS IN JE-ENDEMIC REGIONS

» **Safe and efficacious**
Phase 1 and 2 clinical trials realized in adults have demonstrated the safety and efficacy of our JE Vaccine

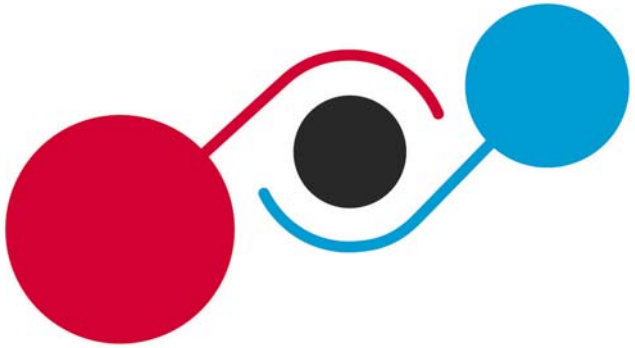
» **Inactivated vaccine versus live vaccine**
Inactivated vaccines have good safety track record

» **Reduced number of doses**
Only two doses are sufficient to obtain a good immunogenicity; Clinical trials with only one dose are planned

» **Formulation adapted to the needs of endemic regions**
A liquid vaccine is more convenient for transport and routine use

Development Outlook

- Phase Strategic alliance between Intercell and Biological E ✓
- Technology transfer ✓
- Clinical development
  start phase 2
  start phase 3
- Licensing & WHO pre-qualification



intercell

SMART VACCINES

For more information be invited to: www.intercell.com